Remarks

Claims 1 and 8 are amended herein. Support for the amendment of claims 1-8 can be found throughout the specification, such as on page 2, lines 7-8; page 7, line 28 and page 13, lines 20-30. Claim 22 is canceled herein. New claims 23-24 are added herein. Support for new claims 23-24 can be found throughout the specification, such as on page 13, lines 18-21.

No new matter is added herein. Reconsideration of the subject application is respectfully requested.

Objection of Claim 22

The Office action objects to claim 22 for an informality. Claim 22 is canceled herein, rendering the rejection moot.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 22 is rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Claim 22 is canceled herein, rendering the rejection moot.

Rejections Under 35 U.S.C. § 103

Claims 1-15 and 22 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jahanshi et al., in view of Binder and further in view of Carruthers et al. Claims 1 and 22 are amended herein to be limited to methods for the treatment of major depression or dysthymia. Applicants respectfully disagree with this rejection as applied to the claims as amended.

Jahanshahi et al. teach that depression in torticollis patients is secondary to the postural abnormality of the head (see page 229, first column), and constitutes "a reaction to the disorder." Botulinium toxin was injected into the superficial neck muscles (not facial muscles) of subjects to treat torticollis (see page 229, second column). The aim of the results presented by Jahanshahi et al. was to assess "improvement of torticollis with botulinum toxin injection accompanied by improvement of depression, reduction of disability, and improvement of the negative body concept and low self esteem" (see page 229, second column). Jahanshahi et al. report that the injection of botulinum toxin into the superficial neck muscles results in straightening of the head and relief from neck pain, and *reduction of depression and disability associated with head*

position and pain (page 231, first column). Jahanshahi et al. conclude that the improvement of depression was a "non-specific result" and that it "provides support for the reactive nature of depression and disability in a proportion of torticollis patients" (page 231, second column). Thus, Jahanshahi et al. only suggest the treatment of subject with a skeletal muscular disorder. Contrary to the assertions made in the Office action (see page 5) Jahanshahi et al. simply do not suggest, nor render obvious the selection of any subject without torticollis, let alone the selection and treatment of a subject with dysthymia or major depression.

Binder teaches the reduction of headache pain by injecting botulinum toxin. Binder et al. suggest the extra-muscular injection of botulinum toxin. Binder et al. do not suggest, nor render obvious, the selection and treatment of any subject with dysthymia or major depression.

Caruthers et al. teach the cosmetic use of botulinum toxin to paralyze the depressor anguli oris muscle to alleviate downturn of a subject's mouth. Caruthers et al. teach the cosmetic effect of botulinum toxin. Caruthers et al. do not suggest the use of a toxin to treat any emotional disorder, let alone a depression or dysthymia.

Examination guidelines have been issued for determining obviousness under 35 U.S.C. § 103 in view of the Supremem Court decision in *KSR International Co. v. Teleflex Inc.* (see the Federal Register, Vol. 72, No. 195, October 10. 2007). There is nothing in the teachings of Jahanshi, on the treatment of toritcollis (a spastic muscle condition of the neck) and injection of botulinum toxin into the neck that would suggest to one of ordinary skill in the art, such as a physician, to combine these teachings with Caruthers et al. on a cosmetic use to alleviate downturn of the mouth. Furthermore, a physician would not look to a headache treatment (such as that taught in Binder) for alleviating cosmetic issues or for treating a severe condition such as torticollis. Thus, there is nothing in the prior art, absent the present specification, that would lead one of skill in the art to combine teachings on the treatment of torticollis with a treatment for a headache or with teachings of how to cosmetically improve the face. Medical treatments used for one of these conditions simply does not prompt variations based on medical treatments used for another condition.

To support a rejection a claim based on combining prior art elements, there must be a finding that the prior art included each element claimed. There is nothing in Jahanshahi et al., Binder et al., or Caruthers et al. that suggests selection of a patient with major depression or a primary mood disorder for treatment with a paralytic agent, such as botulinum toxin.

According to the DSM-IV, a person suffering from Major Depressive Disorder must have a depressed mood or a loss of pleasure in daily activities for at least two weeks. Major Depression is not due to substance abuse or bereavement, nor is it caused by a general medical condition, such as torticollis (see Exhibit A, htpp://depression.about.com/cs/diagnosis/f/mdd.htm). Indeed, Long (Exhibit B, Long, P.W. M.D.,"Major Depressive Disorder," htpp://www.mentalhealth.com/dis1./p21-md01.html) discloses that the symptoms of major depression are NOT due to a physical illness, alcohol, medication, street drugs or normal bereavement (see page 2). Similarly Wikipedia sets forth the conditions of dysthyamia (see Exhibit A, http://en.wikipedia.org/wiki/Dysthymia). Dysthymia is not caused by a general medical condition (such as a muscle spastic condition) or the use of pharmaceutical substances.

In addition, if the teachings of Jahanshahi et al., Binder et al., or Caruthers et al. are combined, there is no evidence that supports that the results obtained with the claimed methods would be predicable. Janhanshahi et al. states that depression secondary to torticollis was alleviated due to straightening of the head. Similarly, Binder et al. teaches the reduction of headaches caused by tension in the muscles of the face. Caruthers et al. teach a better facial expression due to relaxation of the muscles of the mouth. There is nothing that would lead one of skill in the art to predict that a condition without an underlying physical cause could be treated with botulinum toxin. Thus, a *prima facie* case of obviousness simply has not been made based on Jahanshahi et al., Binder et al. and Caruthers et al.

The Office action confirms that the present application (Finzi) has established that "botulinum toxin treats major depression" (see the Office action, page 5) and that the "applicant has presented unexpected superior evidence" (see the Office action, page 8). The documentation of the *unexpected and unpredictable* superior results obtained using the claimed methods overcome any *prima facie* case of obviousness that could be made over the impermissible combination.

Claims 16-21 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jahanshahi et al., Binder et al. and Carruthers et al., further in view of Wagstaff et al.

Wagstaff et al. teach that paroxetine (a selective serotonin reuptake inhibitor, SSRI) is effective at treating depression, obsessive-compulsive disorder, and panic disorder. SSRI

inhibitors are not used to treat the muscle spasms of torticollis or headaches, and are not used for cosmetic purposes.

Jahanshahi et al., Binder et al., and Carruthers et al. are discussed above, both individually and in combination. As discussed above, there is nothing in the teachings of Jahanshi, on the treatment of toritcollis (a spastic muscle condition of the neck) and injection of botulinum toxin into the neck that would suggest to one of ordinary skill in the art, such as a physician, to combine these teachings with Caruthers et al. on a cosmetic use to alleviate downturn of the mouth.

Wagstaff et al., teaches that SSRI inhibitors are of use to treat depression. However, Wagstaff et al. is silent on treatments for toticollis, headache, and cosmetic procedures, as SSRIs would be ineffective for the treatment of torticollis or headache (and would not achieve any a cosmetic effects). Thus, absent the present disclosure, there is nothing to suggest the combination of Wagstaff et al. with Jahanshahi et al., Binder et al., and/or Caruthers et al.

Interestingly, the Office action states that administration of botulinum toxin treats headaches, but admits that headaches "may be caused by administration of the serotonin reuptake inhibitor." Indeed, a physician would not administer one treatment, such as botulinum toxin, designed to treat a specific condition, such as a headache, with another treatment, such as an SSRI inhibitor, which causes that same condition. Thus, Wagstaff et al. teaches away from the combination with Binder et al.

Furthermore, there is no evidence that supports that the results obtained with the claimed methods would be predicable. Janhanshahi et al. states that depression secondary to torticollis, and resulting from muscle spasm, was alleviated by botulinum toxin. Similarly, Binder et al. teaches the reduction of headaches caused by tension in the muscles of the face by botulinum toxin. Caruthers et al. teach a better facial expression due to relaxation of the muscles of the mouth by botulinum toxin. All of the effects observed by Jahanshahi et al., Binder et al. and Caruthers et al. results from muscle paralysis induced by botulimun toxin. However, SSRIs would not affect the muscles of the head or neck. There is nothing that would lead one of skill in the art to predict that the effects of botulinum toxin and SSRIs would act synergistically in a treatment regimen. It is only the present application that describes the use of SSRIs and botulinum toxin in combination.

The specification describes the unexpected superior effect when an SSRI was used in combination with botulinum toxin (see example 2, page 17). Specifically, a subject who was unresponsive to an SSRI responded to treatment with both the SSRI and botulimum toxin. The documentation of the *unexpected and unpredictable* superior results obtained using the claimed methods overcome any *prima facie* case of obviousness that could be made over the impermissible combination. Reconsideration and withdrawal of the rejection are respectfully requested.

Related U.S. Patent Application

Applicants would like to draw the Examiner's attention to U.S. Patent Application No. 11/447,984, filed June 7, 2006, which claims the benefit of a provisional application filed on June 27, 2005. This application is in art unit 1649 and has been assigned to Examiner Dutt. For the Examiner's convenience a copy of this patent application as published (Publication No. 2007/0009555) is attached as Exhibit B.

Conclusion

Applicants believe that this application is in condition for allowance, which action is requested. If any issues remain, the Examiner Ford is formally requested to contact the undersigned prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by a written request.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 595-5301

By _____
Susan Alpert Siegel, Ph.D.
Registration No. 43,121